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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,370	02/19/2002	Marc Alizon	2356-0011-10	2811

22852 7590 08/10/2004

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EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 08/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/076,370	ALIZON ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-28 and 31-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-28 and 31-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the amendment filed 07 April, 2004. Claim 23 was amended and new claims 31-39 introduced. Claims 23-28 and 31-39 are pending in the instant application.

35 U.S.C. § 112, Second Paragraph

Claims 27, 28, 32, and 33 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Two separate requirements are set forth under this statute: (1) the claims must set forth the subject matter that applicants regard as their invention; and (2) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant.

Specifically, the claims are incomplete for omitting essential positive methods steps, such omission amounting to a gap between the steps (refer to M.P.E.P. § 2173.05(q)). *Ex parte Erlich*, 3 U.S.P.Q.2d 1011 (Bd. Pat. App. & Inter. 1986). Claims 27 and 32 are directed toward methods for the detection of antibodies to HIV and neutralizing antibodies to HIV gp120 in an "immunoassay". However, the claimed methodologies fail to set forth any assay steps and provide the requisite reagents that would be required to perform the claimed assay. For instance, immunoassays frequently involve several steps including the following: (i) the attachment of a suitable antigen (e.g., HIV-1 gp120) to a microtiter plate; (ii) the addition of a biological sample from an HIV-1-infected patient; (iii) an incubation period wherein the patient antiserum

is allowed to bind to the immobilized antigen; (iv) a rinsing step to remove unbound immunoglobulin; (v) the addition of labeled anti-Ig antibody to detect the immune complex formed in (iii); (vi) a rinsing step to remove non-specific label; and (vii) a detection step employing enzymatic reagents. Applicants are directed toward pages 32 and 33 for further guidance in drafting the claims.

Claims 28 and 33 are directed toward methods of eliciting neutralizing antibodies by simply "introducing" into a mammal the peptide of interest. These claims are also defective and fail to set forth any meaningful steps that would allow the skilled artisan to practice the claimed invention. Immunization methodologies involve several steps such as the following: (i) preparation of the immunogen in a suitable form (i.e., small peptides may require coupling to a larger molecule such as KLH in order to be immunogenic; appropriate physiological buffers need to be prepared); (ii) the immunogen may frequently require the addition of adjuvant to the composition to ensure the development of a strong and meaningful immune response; (iii) an appropriate immunization regimen needs to be described (i.e., what is the proper dosage, site of adiminstration, boosting regimen, etc.); and, (iv) samples need to be periodically removed from the mammal of interest and assayed for the appropriate affinity and activity using the peptide immunogen and other suitable *in vitro* neutralization assays. Appropriate amendment of the claim language as supported by the disclosure is required.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most

nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-28 and 31-39 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). Claims 23-26 and 31 are directed toward immunogenic HIV-1 Env polypeptides of 5-150 aa comprising at least one amino acid substitution at a specificed position (e.g., aa 8, 9, 90, etc.). Claims 27, 28, 32, and 33 are directed toward methodologies that require these peptides. Claims 34-39 are also directed toward immunogenic HIV-1 Env polypeptides comprising one of the aforementioned substitutions and include additional limitations pertaining to the overall peptide length (e.g., 21 aa, 43 aa, 79 aa, etc.).

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had **possession** of the claimed invention. See, e.g., *Vas-Cath, Inc., v. Mahurkar*, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116. The issue raised in this application is whether the original application provides adequate support for the broadly claimed genus of **immunogenic polypeptide fragments** comprising **HIV-1_{MAL} epitopes** of **5-150 amino acid residues** wherein **at least one amino acid residue is substituted at one of the specified positions.** An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that **fully**

set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. **A biomolecule sequence (e.g., epitope) described only by functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the biomolecule of interest.** *In re Bell*, 991 F.2d 781, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993). *In re Deuel*, 51 F.3d 1552, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995). A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 U.S.P.Q.2d 1895, 1905 (Fed. Cir. 1995). The court noted in this decision that **a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not reasonably lead those skilled in the art to any particular species.**

An applicant may show possession of an invention by disclosure of drawings or **structural chemical formulas** that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or

partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. For some biomolecules, examples of identifying characteristics include a nucleotide or **amino acid sequence**, chemical structure, **binding affinity**, **binding specificity**, and molecular weight. The written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function. Without such a correlation, the capability to recognize or understand the structure from the mere recitation of function and minimal structure is highly unlikely. In the latter case, **disclosure of function alone is little more than a wish for possession; it does not satisfy the written description requirement.** *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1566, 43 U.S.P.Q.2d 1398, 1404, 1406 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998). *In re Wilder*, 736 F.2d 1516, 1521, 222 U.S.P.Q. 369, 372-3 (Fed. Cir. 1984). Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.

Perusal of the disclosure reveals the cloning and characterization of a novel human immunodeficiency virus type 1 originally designated lymphadenopathy associated virus (LAV) MAL, or LAV_{MAL}. A proviral molecular clone was obtained and complete nucleotide isolate of this sequence ascertained (see Figs. 7A-7I). The deduced amino acid sequences of the various viral structural and non-structural genes were also set forth in Figure 7. Specific

envelope polypeptide fragments were set forth on p. 36 of the specification (e.g., 1-530, 34-530, 531-877, 680-700, 37-130, 211-289, 488-530, and 490-620). It should be noted that these designations actually referenced LAV_{BRU} amino acid sequences, not specific LAV_{MAL} polypeptides. Thus, the skilled artisan might conclude that applicants contemplated making and using these specific envelope polypeptides. However, the skilled artisan would not reasonably conclude that applicants were in possession of the claimed invention.

First, **the disclosure fails to identify specific HIV-1_{MAL} immunogenic fragments of the claimed lengths and substitutions.** The specification only sets forth the deduced amino acid sequences of the full-length non-structural and structural genes as set forth in Figure 7 and the specific Env fragments set forth on p. 36. Figure 3 also fails to identify immunogenic MAL peptides. This figure simply provides an amino acid comparison between MAL, BRU, ARV-2, and ELI to assess their genetic relatedness. The figure does not identify or lead the skilled artisan to any particular immunogenic fragment, particularly one carrying amino acid substitutions. Second, **the disclosure fails to perform any type of comparison wherein specific immunogenic fragments from isolate MAL are identified and acceptable amino acid substitutions are performed.** It is well-known in the art that subtle perturbations in an amino acid sequence can profoundly affect both the immunogenic and antigenic properties of any given polypeptide. Thus, the skilled artisan can only hazard a guess as to which substituted MAL fragments will remain immunogenic. Third, **the disclosure fails to provide adequate support for MAL-specific polypeptides the recited lengths (e.g., 21, 43, 79, 94, and 131 aa).** The only numerical limitations set forth in the disclosure recite immunogenic polypeptides or fusion proteins which may

contain between 5 and 150 amino acids (see p. 28). Thus, support does not exist for the current size limitations. Nothing in the disclosure directs the skilled artisan toward any particular MAL immunogenic fragment or any fragment carrying amino acid substitutions. The disclosure fails to identify those molecular determinants modulating the immunogenicity of any given polypeptide fragment. Clearly, the claimed invention simply represents an attempt by applicants to capture subject matter which was neither described nor contemplated at the time of filing. Accordingly, the skilled artisan would reasonably conclude that applicants were not in possession of the claimed invention at the time of filing.

Response to Arguments

Applicants traverse and submit that support for the claimed substitutions can be found in Figures 3E-F. The examiner does not concur with this assessment. Figure 3 provides the amino acid sequence alignment of four different HIV-1 isolates (e.g., BRU, ARV-2, MAL, and ELI). The purpose of this figure is to simply illustrate that while these are all HIV-1 isolates, nevertheless, they display considerable genetic diversity in the envelope region. However, nothing in the figure description of specification examples leads the skilled artisan to any particular peptide with the claimed amino acid substitutions.

Applicants further assert that sufficient support can be found for the claimed size limitations in the disclosure. The passages relied upon fail to provide sufficient support for the claimed size limitations. Nothing in the disclosure references immunogenic Env polypeptides of the claimed lengths (e.g., 21, 43, 79, 94, and 131).

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 9:30 AM to 7:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisors, Laurie Scheiner or James Housel, can be reached at (571) 272-0910 or (571) 272-0902, respectively. Direct general inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Formal communications may be submitted through the official facsimile number which is (703) 872-9306. Hand-carried formal communications should be directed toward the customer window located in Crystal Plaza Two, 2011 South Clark Place, Arlington, VA. Applicants are directed toward the O.G. Notice for further guidance. 1280 O.G. 681. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

07 August, 2004